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Ö. Engin, M. Sayar

published in

*From Computational Biophysics to Systems Biology (CBSB08)*,
Proceedings of the NIC Workshop 2008,
Ulrich H. E. Hansmann, Jan H. Meinke, Sandipan Mohanty,
Walter Nadler, Olav Zimmermann (Editors),
John von Neumann Institute for Computing, Jülich,
NIC Series, Vol. **40**, ISBN 978-3-9810843-6-8, pp. 205-208, 2008.



http://www.fz-juelich.de/nic-series/volume40

# Investigation of Structure of Amphipathic Peptides in Different Environments via Replica Exchange Molecular Dynamics Simulations

**Özge Engin and Mehmet Sayar**

Center for Computational Biology and Bioinformatics, Koc University, 34450, Istanbul, Turkey
*E-mail:* {*ozengin, msayar*}*@ku.edu.tr*

We performed Replica Exchange Molecular Dynamics (REMD) simulation on a 24-residue amphipathic peptide in order to investigate the equilibrium conformational distribution in different environments.The structure of the peptide has been designed such that it adopts a $\beta$-hairpin structure.Experimental findings show that it adapts to $\beta$-hairpin at the air/water interface.It has the amino acid sequence of -KICVRWQYRVQ (D-P) GDICFDVNFDVH- in which D-P and G residues contribute to the formation of a $\beta$-turn structure.We observe that the peptide adapts to coil structure in vacuum whereas it mostly adapts to $\beta$-hairpin in bulk water.At the air/water interface it oriented itself in such a conformation that the hydrophobic residues are lined towards the air, on the other hand, hydrophilic residues are lined towards water.

## 1 Introduction

Amphipathic peptides have alternating hydrophobic and hydrophilic residues in a recurring pattern such that the periodicity in this recursion organizes the non-local interactions among the different types of residues, and this organization among the residues leads to the formation of the type of the overall conformation of the peptide.The equilibrium conformational distribution of amphipathic peptides, as well as others, varies in different environments. Understanding of the probable source of difference in the conformational distribution probabilities is important for both the design of novel peptides and nanomaterials with desired features.

## 2 Methods

REMD simulations[1] for the systems studied were performed with the Gromos 53A6 forcefield[2] implemented in Gromacs (3.3.1) simulation package[3].The SPC216 water model[4]and NVT ensemble were used for all types of simulations. The temperature ranged from 278 K to 320 K in REMD simulations.The exchange probability (computed as the ratio between the successful exchanges and the total number of trials) varied between 10% and 20% for each pair of neighboring replicas; the average exchange probability was approximately 11%, a level ensuring an efficient exploration of the conformational space[1].The water simulation was performed for 80 ns whereas the vacuum simulation was performed for 10 ns.After equilibration was reached, the data was collected and clustered by using the algorithm as described in Daura et. al[5] with the backbone rmsd of 0.15 and 0.20 nm for bulk water and interface simulations, respectively. The secondary structure assignment was made using the STRIDE algorithm[6].

## 3 Results

### 3.1 Vacuum Simulations

The simulation was started from an extended structure, and after approximately 1 ns, it collapsed and remained in a coil structure for the remaining part of the simulation. For this reason, the conformations and the corresponding percentage probability values obtained in vacuum simulation are not given here. These results suggest that the peptide need an assistance of water molecules to adapt to proposed $\beta$-hairpin.

### 3.2 Bulk Water Simulations

The peptide adapts mostly to proposed $\beta$-hairpin in bulk water indicating the importance of water molecules for the formation of that structure.However, it has also preference for other conformations other than this preferred $\beta$-hairpin structure. These conformations emerge as a result of a reduction in the number of intra-molecular hydrogen (H) bonds.These results suggest that water molecules and the number and the residue types in which the H-bonds are made are important for the formation of the $\beta$-turn structure. In this structure $\beta$-turn is constructed by D-Proline and Glycine residues. The top four conformations are given in Fig. 1.

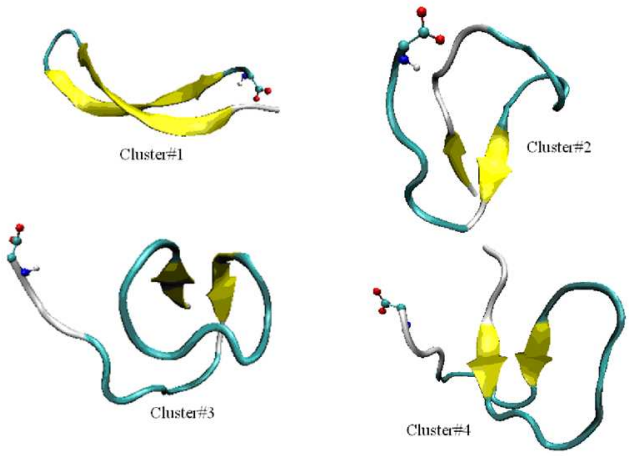


Figure 1. The top four conformations of the peptide obtained upon simulation in bulk water at 300 K. Color codes represent the secondary structure type of each residue. Turn is indicated by green, coil is indicated by white, and sheet structure is indicated by yellow color. The C terminus residues are indicated in CPK representation.

The percentage probability values of these top four conformations are given in Table 1.

| Cluster ID | Cluster1 | Cluster2 | Cluster3 | Cluster4 |
|---|---|---|---|---|
| Probability(%) | 32.0 | 8.0 | 7.84 | 6.0 |

Table 1. The percentage probability values of the top four conformations of the peptide in bulk water at 300 K.

### 3.3 Interface Simulations

The interface simulation was started from a location close to the interface, and the peptide remained there for the rest of the simulation.The top four conformations are given in Fig. 2.

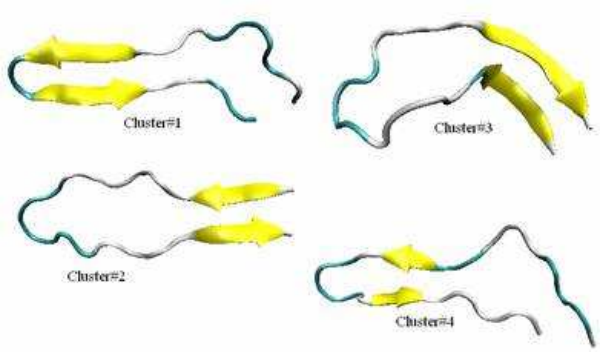


Figure 2. The top four conformations of the peptide obtained upon simulation at the air/water interface at 300 K. Color codes represent the secondary structure type of each residue. Turn is indicated by green, coil is indicated by white, and sheet structure is indicated by yellow color.

The percentage probability values of these top four conformations are given in Table 2.

| Cluster ID | Cluster1 | Cluster2 | Cluster3 | Cluster4 |
|---|---|---|---|---|
| Probability(%) | 41.0 | 27.2 | 7.9 | 7.7 |

Table 2. The percentage probability values of the top four conformations of the peptide at the interface at 300 K.

The peptide was aligned parallel to the interface, and it was orientated in such a way that the hydrophobic residues were lined towards the air whereas both the hydrophobic and hydrophilic residues were lined towards water as shown in Fig. 3. However, these are still preliminary results; the equilibrium has not been reached yet.

## 4 Conclusion and Future Work

We identified the equilibrium conformational distributions of a 24-residue amphipathic peptide via REMD simulations in vacuum, bulk water, and at air/water interface.The peptide adapts to different conformations in different environments. Understanding of the be-

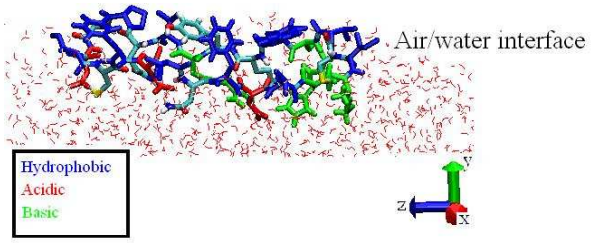


Figure 3. The orientation of residues at the air/water interface. The hydrophobic residues are colored in blue, basic residues are colored in green and the acidic residues are colored in red.

havior of peptides in different environments will help design of novel peptides and nanomaterials with desired features.We are also simulating different amphipathic peptides having different amino acid sequence to investigate the effect of residue specificity on the formation of overall conformations of peptides.Moreover, we are planning to make simulations at interface with larger number of peptides to understand the behavior of both inter and intra molecular interactions.

## Acknowledgments

We thank Raymond Tu and his group for scientific discussions, and sharing their experimental results on the peptide molecule. We also thank to Berk Hess and Alessandra Villa for their scientific discussion. This research is supported by grants from TUBITAK (106T575), and Partner Group of Max-Planck Institute for Polymer Research.

## References

1. Y.Sugita and Y.Okamoto, *Replica-exchange molecular dynamics method for protein folding*, Chem.Phys.Lett. **314**, 141, 1999.
2. C. Ooestenbrink,A. Villa,A. Mark and W. F. Gunsteren, *A Biomolecular Force Field Based on the Free Enthalpy of Hydration and Solvation:The GROMOS Force-Field Parameter Sets 53A5 and 53A6*, J. Comp.Chem **25**, 1656, 2004.
3. D. Spoel, A. R. Buuren,E. Meulenhoff,D.P. Tieleman, A. Sijbers,B. Hess, K. Feenstra, E. Lindahl, R. Drunen, and H. Berendsen, *Gromos User Manual Version 3.3.1* (Nijenborgh 4, 9747 AG Groningen, The Netherlands, www.gromacs.org, 2002).
4. H. J.C Berendsen,J. P. Postma, W. F. van Gunsteren, A. DiNola, J. R. Haak, *Molecular Dynamics with Coupling to an External Bath*, J. Chem. Phys. **81**, 3684, 1984.
5. X. Daura, K. Gademann, B. Jaun, D. Seebach, W. F. van Gunsteren, A. E. Mark, *Peptide folding: When simulation meets experiment*, Angew. Chem. Int. Ed. **18**, 236, 1999.
6. D. Frishman and P. Argos, *Knowledge-based secondary structure assignment*, Proteins: Structure, Function and Genetics **23**, 566, 1995.